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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventors	:	Walker	Group Art Unit :	1647
Appl. No.	:	09/065,330	Confirmation No.:	7326
Filed	:	April 23, 1998	Customer Number:	25213
For	:	PROLACTIN ANTAGONISTS AND USES THEREOF		
Examiner	:	Christine J. Saoud		

DECLARATION UNDER 37 C.F.R.§ 1.132

United States Patent and Trademark Office
P.O. Box 2327
Arlington, Virginia 22202

Dear Sir:

I, Charles Clevenger, M.D., Ph.D., do hereby declare and say as follows:

1. I am an Associate Professor in the Department of Pathology and Laboratory Medicine at the University of Pennsylvania. My scientific work includes research on prolactin, prolactin receptors, and other hormones. I have published over 50 scientific articles, reviews and book chapters related to my work on prolactin, prolactin receptors and other hormones. My scientific curriculum vitae is enclosed as Exhibit A and forms part of this declaration.

2. I have read and understand the above-identified patent application "PROLACTIN ANTAGONISTS AND USES THEREOF" Serial No. 09/065,330. In particular, I have read and understand the claims pending in this application. I understand that the claimed invention is directed to a recombinant molecule encoding a prolactin variant mutated at amino acid residue 179 (for human prolactin; or mutated at an equivalent residue for prolactin of a different species) that mimics phosphorylated prolactin for that species by being capable of antagonizing the growth-promoting effects of non-phosphorylated prolactin in that species. I understand that the claimed invention is further directed to compositions containing such recombinant molecules encoding prolactin mutated at amino acid residue 179 (or at an equivalent residue for prolactin of a different species).

3. I have read and understand the references Cooke et al. (U.S. Patent 4,725,549), Walker (Trends in Endocrinology and Metabolism, 5(5):195-200 (1994)) and Maciejewski et al. (J. of Biological Chemistry, 270(46): 27661-27665 (1995)). In particular, I understand that Cooke et al. describes the cloning and expression of a DNA encoding prolactin, and discusses the recombinant production of prolactin. I understand that Walker mentions that threonine 63 and serine 177 are conserved in prolactins of different species (page 196, column 3), that "these regions of the molecule have also been demonstrated to be critical for biological activity" (page 196, column 3), and that non-phosphorylated prolactin antagonizes the growth-promoting action of prolactin (page 197, column 2). I further understand that Walker also states that "[w]hether this superantagonism is achieved by a much increased affinity for the receptor of initiation of a different signal cascade within the cell is unknown at present" (page 197, column 2).

4. I have read and understand the Office Action issued by the Patent Examiner on January 8, 2003 regarding the above-identified patent application.

5. I understand that the Patent Examiner has rejected the pending claims, saying that these claims would be obvious if one were to combine the teachings of Cooke et al., Walker, and Maciejewski et al. In particular, I understand that the Patent Examiner suggests that Maciejewski's experiments substituting amino acid residue 90 of bovine prolactin, combined with Walker's statement that serine 177 in rat prolactin is critical for biological activity, makes obvious the substitution of amino acid residue 179 of human prolactin that is claimed in the subject patent application. Referring to human prolactin amino acid residue 179, the Examiner states "one of ordinary skill in the art would also expect that substitution of this position with glutamic acid would result in mimicry of the phosphorylation as found in the bovine prolactin."

6. I have read and considered the arguments and conclusions presented by the Patent Examiner. It is my considered scientific opinion that these references do not make obvious that substitution of amino acid residue 179 of human prolactin would result in a variant that mimics phosphorylated prolactin capable of antagonizing the growth promoting effects of non-phosphorylated prolactin, for the reasons discussed below.

7. Maciejewski et al. report on the results of experiments with bovine prolactin in which serine residues at positions 26, 34 and 90 have been substituted by glutamic acid (page 27662, column 1, line 29). These results indicate that replacement of each of these serine residues by glutamic acid produces structural changes in bovine prolactin (page 27664, column 2, lines 37-38). In addition, Maciejewski's results indicate that glutamic acid substitution of serine 90 in bovine prolactin results in a protein having reduced activity similar to phosphorylated prolactin receptor (page 27663, column 3, line 10 to page 27664 column 1, line 1; page 27664 column 2, lines 44-45). However, Maciejewski et al. also report that replacement of serine residues 26 and 34 with glutamic acid does not affect biological activity (page 27664, column 2, lines 43-44).

8. Given the high degree of identity and similarity in the primary sequence between prolactin an growth hormone (Cooke et al), and the recognized crystal structure of growth hormone (Nature 372:478, 1994), the location of the serine 90 residue in bovine prolactin may have been anticipated to reside in a flexible peptide loop between two alpha helices. In contrast, the serine 179 residue in human prolactin may have been anticipated to be buried in the hydrophobic alpha helical core of human prolactin; findings that have been recently confirmed by NMR (J Mol Biol 328:1105, 2003). Thus, any one of "ordinary skill" would anticipate that mutations at these sites would have significantly different effects. Furthermore, comparison of the functional antagonism data presented in the Maciejewski et al. manuscript in comparison to the data presented by Walker et al in their patent application demonstrated significant functional differences between the bovine S90 mutant and the human S179 mutant; namely that the bovine S90 mutant is a weak antagonist, while the S179 mutant is a super-antagonist.

9. Thus, it is my considered scientific opinion that, based on the disclosures of Cooke et al., the Walker 1994 article, and the Maciejewski et al. paper, one could not predict the biological effects of an experimental mutation in bovine prolactin replacing a serine residue with a glutamic acid residue without actually making and testing that mutant prolactin.

10. None of the cited references discuss substituting serine 179 to mimic non-phosphorylated prolactin. Neither Cooke et al. nor Walker 1994 discuss substitution of amino acid residue 179 of human prolactin. In particular, Maciejewski et al. do not mention residue 179 of either bovine or human prolactin, nor did Maciejewski et al. perform experiments replacing residue 179 of bovine or human prolactin.

11. Thus, it is my considered scientific opinion that the teachings of Maciejewski et al., even if combined with the disclosures of Walker 1994 and of Cooke, would not have enabled one of ordinary skill in the art at the time to predict using established scientific rationale the effects of amino acid substitutions at residue 179 of human prolactin or of prolactin of other species based on known structural and functional differences between residues 90 (in bovine PRL) and 179 (in human PRL). It is thus my considered scientific opinion that one of ordinary skill in the art at the time would not have expected that substitution in human PRL of serine residue 179 with glutamic acid would produce a mimic of naturally phosphorylated prolactin that would be capable of super-antagonizing the growth promoting effects of non-phosphorylated prolactin.

12. I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true. I declare that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

5/23/03
Date

Charles Clevenger, M.D., Ph.D.

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5/23/03 4:30 PM (39754.0611)

Date: 5/03

University of Pennsylvania School of Medicine

CURRICULUM VITAE

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Philadelphia, PA 19104
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Education:

1978-80	B.S., 1982, Honors Program in Medical Education, Northwestern University, Evanston, IL
1980-87	M.D., 1987, Northwestern University Medical School, Chicago, IL
1982-85	Ph.D., 1986, Tumor Cell Biology Program, Northwestern University Medical School, Chicago, IL

Postgraduate Training and Fellowship Appointments:

1987-1990	Resident, Department of Pathology & Laboratory Medicine, Hospital of the University of Pennsylvania, Philadelphia, PA
1991	Fellow in Cytopathology, Department of Pathology & Laboratory Medicine, Hospital of the University of Pennsylvania, Philadelphia, PA

Military Service: None

Faculty Appointments:

1987-1991	Assistant Instructor, Department of Pathology & Laboratory Medicine, University of Pennsylvania, School of Medicine, Philadelphia, PA
1992-1999	Assistant Professor, Department of Pathology & Laboratory Medicine, University of Pennsylvania, School of Medicine, Philadelphia, PA
1999-Present	Associate Professor (h.M.A., with tenure), Department of Pathology & Laboratory Medicine, University of Pennsylvania, School of Medicine, Philadelphia, PA

Hospital and Administrative Appointments:

1992-2002	Director, DNA Flow Cytometry Facility, Department of Pathology & Laboratory Medicine, University of Pennsylvania Medical Center
1992-Present	Staff, Cytopathology Section, Department of Pathology & Laboratory Medicine, University of Pennsylvania Medical Center
2001-Present	Residency Program Co-Director, Department of Pathology & Laboratory Medicine, University of Pennsylvania Medical Center

Specialty Certification:

1991	Anatomic Pathology Boards (#91-455)
1993	Added Qualification in Cytopathology (#AQ 93-045)

Licensure: Pennsylvania Unrestricted Medical License MD-044531-E

Charles V. Clevenger, MD, PhD

Awards, Honors and Membership in Honorary Societies:

2003	Pfizer Outstanding Investigator Award, American Society for Investigative Pathology
2003	American Society for Clinical Investigation
1995	American Cancer Society Junior Faculty Research Award
1989	Experimental Pathologist-In-Training Award, American Society for Investigative Pathology
1987	Graduation with Distinction, Northwestern University Medical School
1982	Alpha Omega Alpha

Memberships in National Professional and Scientific Societies:

American Association for Cancer Research
American Association of University Pathologists
American Society for Cell Biology
American Society for Investigative Pathology
Endocrine Society
Pituitary Society
United States & Canadian Academy of Pathology

Editorial Positions:

-Editorial Board Member, *Journal of Histochemistry and Cytochemistry* (`92-`96).
-Editorial Board Member, *Endocrinology* (`97-`00).
-Referee, (past 5 years): *American Journal of Pathology* (1996-`01), *Arthritis and Rheumatism* (`00), *Biochimica et Biophysica Acta* (`97-98), *Blood* (`02), *British Journal of Cancer* (`00-02), *Cancer* (`91-00), *Cancer Research* (`92-03), *Cancer Letters* (`99-00), *Cellular Immunology* (`00), *Clinical Cancer Research* (`01), *Clinical Immunology* (`03), *Cytometry* (`88-98), *Endocrine* (`99), *Endocrinology* (`95-03), *DNA and Cell Biology* (`99), *International Journal of Cancer* (`95-02), *Journal of Biological Chemistry* (`96-00), *Journal of Clinical Endocrinology and Metabolism* (`96-02), *Journal of Clinical Investigation* (`02), *Journal of Endocrinology* (`99-02), *Journal of Neuroendocrinology* (`99), *Molecular and Cellular Endocrinology* (`99-00), *Molecular Endocrinology* (`92-03), *Nature* (`01), *Oncogene* (`01), *Proceedings of the Society for Experimental Biology and Medicine* (`99), *Protein Engineering* (`01), *Reproduction, Fertility, and Development* (`02).

Service to the Scientific Community:

Study Sections

-Basic Breast Biology Study Section Member, California Breast Cancer Research Program (1996-1998).
-Cell Biology Study Section Member, Dept. of Defense Breast Cancer Research Program (1996).
-Cell and Mol Biology Study Section Member, Dept. of Defense Ovarian Cancer Research Program (1998, 2000).
-Endocrinology Study Section Member, Dept. of Defense Breast Cancer Research Program (2001-03).
-Canadian Breast Cancer Research Initiative Site Visit Member (2000).
-NIH *Ad hoc* Study Section Member, Biochemical Endocrinology (BCE; 10/01, 6/02).
-NIH *Ad hoc* Study Section Member, Reproductive Endocrinology (REN; 2/, 6/, & 10/02).
-NIH *Ad hoc* Special Emphasis Panel, Experimental Therapeutics (ZRG1 ET-2; 4/02).
-NIH P01 *Ad hoc* Study Section Member (5/02; 2/03; NCI-D-GRB-M(B1)).
-NIH Permanent Study Section Member, Reproductive Endocrinology (REN; 2003-).
-NIH *Ad hoc* Special Emphasis Panel, Reproductive Biology Sciences (ZRG1 REB; 3/03).

Other Responsibilities

-Minisymposium Chair ("Gene expression in neoplasia"), 1997 FASEB Meeting.
-Oral Symposium Chair (Prolactin), 1998 Endocrine Society Meeting.
-Symposium Chair (Novel Actions of Pituitary Hormones), 5th International Pituitary Congress (1998).

-Faculty, National Clinical Course on Flow and Image Cytometry, Dartmouth Medical School (1999).
-Endocrine Society Media Expert on Breast Cancer (1999-).
-Scientific Advisory Board Member, NIH Cooperative Human Tissue Network (2000).
-Symposium Chair (Hormones, Immunity and Health), 2001 Endocrine Society Meeting.
-Member, US & Canadian Academy of Pathology, Castleman Award Committee (2003-6).
-Research Fellowship Assessor, Australian National Health and Medical Research Council (NHMRC; 2003)

Academic Committees (University of Pennsylvania):

1996	Admissions Interviewing Committee, Graduate Group in Immunology
1997-01	Special Events Committee, Chair, Graduate Group in Immunology

Principal Investigator of Grants (Past 5 years; Total Direct Costs):

Previous:

1993-1997	"Characterization of Prolactin Receptor Function in T Lymphocytes", NIH R29 AI33510, $350,000.
1995-1998	"Characterization of Prolactin Receptor in Breast Cancer", ACS JFRA-588, $90,500.
1996-1999	"Autocrine Function of Prolactin in Breast Cancer", NIH 1R01 CA69294, $341,000.
1996-2000	"Mechanisms of Prolactin Receptor Signaling by Vav", NIH 1R01 DK50771, $432,620.
1999-2002	"Function of the Prolactin Receptor Complex in Breast Cancer", NIH 2R01 CA69294, $456,000.

Current:

2000-2003	"Cyclophilin B in Prolactin Transport and Function", ACS RPG00307-01TBE, $300,000.
2001-2006	"Multimeric Signaling Complexes in PRLr Transduction", NIH 1R01 CA92265, $875,000.
2002-2007	"Function of the Prolactin Receptor Complex in Breast Cancer", NIH 2R01 CA69294, $875,000.

Pending

2003-2008	"Regulation of Stat Function in Breast Cancer", NIH 1R01 102682, $1,125,000 (Percentile: 13.5)

Patents

"Use of cyclophilin B and mutations thereof as modulators of somatolactogenic functions"; CV Clevenger and MA Rycyzyn; University of Pennsylvania Docket #L1951, Patent Pending.
"Characterization and Use of a Human Prolactin Binding Protein (hPRLBP)", CV Clevenger and JB Kline; University of Pennsylvania Docket #N2491, Patent Pending.

Lectures by Invitation (past 4 years):

January, 1999	"Novel mechanisms of prolactin receptor signaling", Research Seminar Series, Department of Pathology, Dartmouth Medical College, Lebanon Junction, NH.
February, 1999	"Novel mechanisms of prolactin receptor signaling", Research Seminar Series, Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, PA.
March, 1999	"Mechanisms of Prolactin Signaling: Novel Insights into Peptide Hormone Action", Research Seminar Series, Cleveland Clinic, Cleveland, OH.
April, 1999	"Novel mechanisms of prolactin receptor signaling", Research Seminar Series, Department of Pathology, University of Alabama School of Medicine, Birmingham, AL.
June, 1999	"Mechanisms of prolactin receptor signaling – relevance to human breast cancer", Pathology Rounds, Emory University Medical Center, Atlanta, GA.
August, 1999	"Novel mechanisms of prolactin transduction in hormone dependent malignancies", Guest Lecturer, MD Anderson Cancer Center, Houston, TX.
September, 1999	"Mechanisms of autocrine/paracrine prolactin function within the breast", Invited Symposia speaker, European Union Meeting (COST Action) on Mammary Gland Biology, Tours, France.

October, 1999	"Novel mechanisms of prolactin transduction in cells of the immune system - Role of cyclophilin B", Invited Symposia speaker, IVth Congress of the International Society of Neuroimmunomodulation, Lugano, Switzerland.
February, 2000	"Role of cyclophilin B in somatolactogenic transduction and nuclear retrotranslocation", Invited Symposium Presentation, Gordon Conference on Prolactin, Ventura, CA.
March, 2000	"Prolactin and the immune system", Invited speaker, 19th Joint Meeting of the British Endocrine Societies, Manchester, England.
March, 2000	"Novel mechanisms of prolactin transduction", Dept. of Molecular Biology Rounds, Autonomous University of Madrid, Madrid, Spain.
April, 2000	"Novel actions of prolactin in human breast cancer", Endocrinology Grand Rounds, University of Massachusetts, Worcester, MA.
April, 2000	"Intranuclear signaling by prolactin mediated by cyclophilin B", Invited minisymposium (Role of Polypeptide Growth Factors in the Nucleus) presentation, EB 2000 meeting, San Diego, CA.
April, 2000	"Role of the prolactin receptor complex in human breast cancer", Invited minisymposium (Breast Cancer) presentation, EB2000 meeting, San Diego, CA.
June, 2000	"Nuclear effects of prolactin", Invited symposium presentation, 81st meeting of the Endocrine Society, Toronto, Canada.
October, 2000	"Genomic and non-genomic actions of prolactin: Relevance to breast cancer". Invited Seminar Series Presentation, Armed Forces Institute of Pathology, Washington, DC.
January, 2001	"Genomic and non-genomic actions of prolactin in the pathogenesis of human breast cancer", Cancer Center Grand Rounds, Emory University.
June, 2001	"Genomic and non-genomic actions of prolactin". Invited symposium presentation, Gordon Conference on Mammary Gland Biology, Bristol, RI.
October, 2001	"Genomic and non-genomic actions of prolactin in breast cancer", Invited plenary presentation, COMBIO 2001, Canberra, Australia [canceled].
October, 2001	"Intranuclear actions of polypeptide hormones". Invited symposium presentation, COMBIO 2001, Canberra, Australia [canceled].
January, 2002	"Novel functions and signaling pathways of the prolactin/prolactin receptor complex". Invited presentation, Bristol/Meyers/Squibb, Princeton, NJ.
February, 2002	"Regulation of PRL-induced transcription by prolyl isomerases" Invited symposium presentation, Gordon Conference on Prolactin, Ventura, CA.
February, 2002	"Do PRL and GH cause cancer?", Invited debator, Gordon Conference on Prolactin, Ventura, CA.
December, 2002	"Mechanisms of prolactin action in reproduction", Grand Rounds, Dept of Ob/Gyne, University of Pennsylvania.
March, 2003	"Novel paradigms of peptide hormone signal transduction in breast and prostate cancer", Dept. of Cell Biology Seminar Series, Georgetown University, Washington, DC.
April, 2003	"Novel paradigms of signal transduction in breast cancer", invited ASIP Pfizer Award Plenary Lecture, Experimental Biology 2003, San Diego, CA.

Bibliography:

Original Research Publications, peer reviewed:

1. **Clevenger CV**, Epstein AL: Identification of a nuclear protein component of interchromatin granules using a monoclonal antibody and immunogold electron microscopy. *Exp Cell Res* 151:194-207, 1984.
2. **Clevenger CV**, Epstein AL: Use of immunogold electron microscopy and monoclonal antibodies in the identification of nuclear substructures. *J Histochem Cytochem* 32:757-765, 1984.
3. Murao SI, Epstein AL, **Clevenger CV**, Huberman E: Expression of maturation specific nuclear antigens in differentiating human myeloid and monocytic leukemia cells. *Cancer Res* 45:791-795, 1985.
4. **Clevenger CV**, Epstein AL, Bauer KD: A method for simultaneous nuclear immunofluorescence and DNA content quantitation using monoclonal antibodies and flow cytometry. *Cytometry* 6:208-214, 1985.

5. Bauer KD, **Clevenger CV**, Williams TJ, Epstein AL: Assessment of proliferation-dependent antigen expression using multiparameter flow cytometry and antibody-acridine orange sequential staining. *J Histochem Cytochem* 34:245-250, 1986.
6. Bauer KD, **Clevenger CV**, Williams TJ, Murad T, Epstein Al, Scarpelli DG: Simultaneous nuclear antigen and DNA content quantitation using paraffin-embedded colonic tissue and multiparameter flow cytometry. *Cancer Res* 46:2428-2434, 1986.
7. **Clevenger CV**: Characterization of the proliferation associated nuclear antigen p105. Ph.D. Dissertation, 1986.
8. **Clevenger CV**, Epstein AL, Bauer KD: Modulation of the nuclear antigen p105 in lymphocytes as a function of cell cycle progression. *J Cell Physiol* 130:336-343, 1987.
9. **Clevenger CV**, Epstein AL, Bauer KD: Quantitative analysis of a nuclear antigen in interphase and mitotic cells. *Cytometry* 8:280-286, 1987.
10. Epstein AL, Samoszuk M, Stathopoulos E, Naeve GS, **Clevenger CV**, Weil S, Marder RJ: Immunohistochemical characterization of a 183 kiloDalton myeloid specific DNA-binding protein in B5 fixed, paraffin-embedded tissues and bone marrow aspirates by monoclonal antibody BM-1. *Blood* 70:1124-1130, 1987.
11. Bronner MP, **Clevenger CV**, Edmonds PR, Lowell DM, McFarland MM, LiVolsi VA: Flow cytometric analysis of DNA content in Hurthle cell adenomas and carcinomas of the thyroid. *Am J Clin Pathol* 89:764-769, 1988.
12. **Clevenger CV**, Russell D, Shipman P, Prystowsky M: Regulation of IL2-driven T-lymphocyte proliferation by prolactin. *Proc Natl Acad Sci USA*, 87:6460-6464, 1990.
13. **Clevenger CV**, Sillman AL, Prystowsky MB: Interleukin-2 driven nuclear translocation of prolactin in cloned T-lymphocytes. *Endocrinology*, 127:3151-3160, 1990.
14. **Clevenger CV** and Shaw LM: Colchicine poisoning: Report of a fatal case with body fluid analysis by GC/MS and histopathologic examination of postmortem tissues. *J Anal Toxicol*, 15:151-154, 1991.
15. **Clevenger CV**, Altmann SW, Prystowsky MB: Requirement of nuclear prolactin for interleukin-2-stimulated proliferation of T lymphocytes. *Science*, 253:77-79, 1991.
16. **Clevenger CV**, Sillman AL, Hanley-Hyde J, Prystowsky MB: Requirement for prolactin during cell cycle regulated gene expression in cloned T lymphocytes. *Endocrinology*, 130:3216-3222, 1992.
17. Tumas K, Overmoyer B, **Clevenger CV**, Blank KJ, Prystowsky MB: Murine leukemia virus infection in immunocompetent adult mice. *Virology*, 192:1-10, 1993.
18. Prystowsky JH, **Clevenger CV**, Zheng Z-S: Inhibition of ornithine decarboxylase activity and cell proliferation by ultraviolet B radiation in EGF-stimulated cultured human epidermal keratinocytes. *J Invest Dermatol*, 101:54-58, 1993.
19. Aird F, **Clevenger CV**, Prystowsky MB, Redei E: Corticotropin-releasing factor mRNA in rat thymus and spleen. *Proc Natl Acad Sci USA*, 90:7104-7108, 1993.
20. Prystowsky JH, **Clevenger CV**, Zheng Z-S: Epidermal growth factor induces ornithine decarboxylase in SV40 immortalized human keratinocytes. *Exp Dermatol*, 2:125-132, 1993.
21. **Clevenger CV**, Torigoe T, Reed JC: Prolactin induces the rapid phosphorylation and activation of the prolactin receptor associated Raf-1 kinase in a T-cell line. *J Biol Chem*, 260:5559-5565, 1994.
22. **Clevenger CV** and Medaglia MV: The protein tyrosine kinase $p59^{fyn}$ is associated with prolactin receptor and is activated by prolactin stimulation of T-lymphocytes. *Mol Endocrinol*, (Issue's featured Cover Art), 8:674-681, 1994.
23. **Clevenger CV,** Chang W-P, Ngo W, Pasha LM, Montone KT, Tomaszewski JE: Expression of prolactin and prolactin receptor in human breast carcinoma: Evidence for an autocrine loop. *Am J Pathol*, 146:695-705, 1995.
24. **Clevenger CV,** Ngo W, Sokol DL, Luger SM, Gewirtz AM: Vav is necessary for prolactin-stimulated proliferation and is translocated into the nucleus of a T-cell line. *J Biol Chem,* 270:13246-13253, 1995.
25. Luger SM, Ratajczak J, Ratajczak MZ, Kuczynski WI, DiPaola RS, Ngo W, **Clevenger CV**, Gewirtz AM: A functional analysis of protooncogene Vav's role in adult human hematopoiesis. *Blood*, 87:1326-1334, 1996.
26. Chang W-P and **Clevenger CV**: Modulation of growth factor receptor function by isoform heterodimerization. *Proc Natl Acad Sci USA,* 93:5947-5952, 1996.
27. Tumas-Brundage KM, Garret W, **Clevenger CV**, Blank K, Prystowsky MB: Murine leukemia virus infects early bone marrow progenitors in immunocompetent mice. *Virology* 224: 573-575, 1996.
28. **Clevenger CV** and Plank TL: Prolactin as an autocrine/paracrine factor in breast tissue. *J Mammary Gland Biology and Neoplasia*, 2:59-68, 1997.
29. **Clevenger CV,** Thickman K, Ngo W, Chang W-P, Takayama S, Reed JC: Role of Bag-1 in the survival and proliferation of the cytokine-dependent lymphocyte lines, Ba/F3 and Nb2. *Mol Endocrinol*, 11:608-618, 1997.

30. Reynolds C, Montone KT, Powell CM, Tomaszewski JE, **Clevenger CV**: Distribution of prolactin and its receptor in human breast carcinoma. *Endocrinology*, 138:5555-5560, 1997.
31. Chang W-P, Ye Y, **Clevenger CV**: Stoichiometric structure/function analysis of the prolactin receptor signaling domain by receptor chimeras. *Mol Cell Biol*, 18:896-905, 1998.
32. **Clevenger CV**, Freier DO, and Kline JB: Function of the prolactin receptor complex in the immune system. *J Endocrinol,* 157:187-197, 1998.
33. Krajewska M, Krajewski S, Zapata JM, Van Arsdale T, Gascoyne R, Shabaik A, Hugh J, Reynolds C, **Clevenger CV**, Reed JC: TRAF-4 expression in epithelial progenitor cells: Analysis in normal adult, fetal, and tumor tissues. *Amer J Pathol,* 152:1549-1561, 1998.
34. Bell KA, Van Deerlin VMD, Addya K, **Clevenger CV**, Van Deerlin PG, Leonard DGB: Molecular genetic testing from paraffin-embedded tissue distinguishes non-molar hydropic abortion from hydatidiform mole. *Mol Diagnosis,* 4:11-19, 1999.
35. Maus MV, Reilly SC, **Clevenger CV**: Prolactin as a chemoattractant for human breast cancer. *Endocrinology*, 140: 5447-5450, 1999.
36. Kline JB, Roehrs H, **Clevenger CV**: Functional characterization of the intermediate isoform of the human prolactin receptor. *J Biol Chem*, 274:35461-35468, 1999.
37. Rycyzyn MA, Reilly SC, O'Malley K, **Clevenger CV**: Role of cyclophilin B in prolactin signal transduction and nuclear retrotranslocation. *Molecular Endocrinology,* 14: 1175-1186, 2000.
38. Kline JB, Moore D, **Clevenger CV**: Activation and association of the Tec tyrosine kinase with the prolactin receptor: Mapping of a Tec/Vav – receptor binding site. *Molecular Endocrinology,* 15:832-841, 2001.
39. Kline JB and **Clevenger CV**: Identification and characterization of the prolactin binding protein (PRLBP) in human serum and milk. *J Biol Chem*, 276: 24760-24766, 2001.
40. Rycyzyn MA and **Clevenger CV**: The intranuclear prolactin/cyclophilin B complex as a transcriptional inducer. *Proc Natl Acad Sci, USA,* 99:6790-6795, 2002.
41. Kline JB, Rycyzyn MA, **Clevenger CV**: Characterization of a novel and functional human prolactin receptor isoform (ΔS1PRLr) containing only one extracellular fibronectin-like domain. *Molecular Endocrinology,* 16:2310-2322, 2002.
42. Syed F, Rycyzyn MA, Westgate, L, **Clevenger CV**: A novel and functional interaction between cyclophilin A (CypA) and the prolactin receptor. *Endocrine,* 20:83-90, 2003.
43. Yuan CM, **Clevenger CV**, McCarthy T, McCoy CS, Herbert D, Yoo J, Bagwell B, Moore JS: "Adjusting" to the new role of DNA analysis in breast cancer prognosis. Submitted.
44. DeMaria J, Freier DO, **Clevenger CV**: Functional interaction of the Nek3 kinase with the Vav2 guanine nucleotide exchange factor. In preparation.
45. Thompson CJ, **Clevenger CV**, Kline JB, Ho S-M: Identification of a novel prolactin receptor isoform and its overexpression in an androgen-independent prostate tumor. In preparation.

Abstracts (of work not yet published):

1. Gadd SL and **Clevenger CV**: Ligand-independent complex formation of the prolactin receptor. Presented at the 85th Meeting of the Endocrine Society, Philadephia, PA 2003.
2. Miller SL, DeMaria JE, Riegel AM, **Clevenger CV**: The role of Nek3 in prolactin-mediated Vav2 function in human breast cancer. Presented at the 85th Meeting of the Endocrine Society, Philadephia, PA 2003.
3. Haubein LN, Rycyzyn MA, **Clevenger CV**: Regulation of Stat5 function by c-myb. Presented at the 85th Meeting of the Endocrine Society, Philadephia, PA 2003.
4. Gadd SL, LiVolsi VA, **Clevenger CV**: Nuclear localization of the human prolactin receptor. Presented at the 85th Meeting of the Endocrine Society, Philadephia, PA 2003.

Charles V. Clevenger, MD, PhD

Editorials, Reviews, Book Chapters (Peer and Non-Peer Reviewed):

1. Epstein AL, **Clevenger CV**: Identification of nuclear antigens in human cells by immunofluorescence, immunoelectron microscopy, and immunobiochemical methods using monoclonal antibodies. In: *Recent Advances in Non-histone Protein Research*, Beckhor, I. (ed), CRC Press, Boca Raton, FL Volume 1:117-137, 1985
2. **Clevenger CV**: Utility of clinical flow cytometry. *Surgical Pathology* 2(1):1-2, 1989.
3. **Clevenger CV** and Shankey TV: Cytochemistry II: Immunofluorescence measurement of intracellular antigens. In: *Clinical Flow Cytometry: Principles and Clinical Application*, Bauer KD, Duque RE, Shankey TV eds., Williams and Wilkins, Baltimore, MD, Chapter 10, pgs. 157-175, 1992.
4. Prystowsky MB and **Clevenger CV**: Prolactin as a second messenger for interleukin 2. In: *Immunomethods*, Blalock JD, ed., Academic Press, San Diego, CA, 5:49-55, 1994.
5. **Clevenger CV**: Role of tubulin-associated G-proteins during mitosis. *Lab Invest* 71:155-157, 1994.
6. Buckley A, **Clevenger CV**, Prystowsky MB: Nuclear prolactin: A physiologically relevant site of hormone action. *Endocrine News,* 20:2, 1995.
7. Buckley AR, Cerletty JM, and **Clevenger CV**: Targeted expression of the *ret*/PTC1 oncogene induces papillary thyroid carcinomas, by Jhiang SM et al: Commentary. *Endocrine News*, 21:3-5, 1996
8. ***Clevenger CV**: DNA content analysis of thyroid neoplasms. *Pathology Case Reviews*, 2:235-240, 1997.
9. **Clevenger CV** and LiVolsi AL: The breast. In: *Functional Endocrine Pathology, 2nd ed.,* Kovacs K and Asa S, eds., Blackwell Science, Inc., Cambridge, MA, Chapter 24, pgs 715-732, 1998.
10. **Clevenger CV** and Flanagan-Cato L: Neuroendocrine immunology. In: *Neuroendocrinology in Physiology and Medicine, 1st ed.,* Conn PM and Freeman M, eds., Humana Press, Inc., Totowa, NJ, Chapter 29, pgs 509-525, 1999.
11. **Clevenger CV** and Rycyzyn MA: Translocation and action of polypeptide hormones within the nucleus: Relevance to lactogenic transduction. In: *Biology of the Mammary Gland*, Clegg RA and Mol J, eds., Kluwer/Plenum Publishers, New York, NY, Chapter 9, pgs 77-84, 2000.
12. Rycyzyn MA and **Clevenger CV:** Role of cyclophilins in somatolactogenic action. *Annals NY Acad of Sciences*, 917: 514-521, 2001.
13. **Clevenger CV**, Rycyzyn MA, Syed F, and Kline JB: Prolactin receptor signal transduction. In: *Prolactin*. Horseman, ND, ed., Kluwer Publisher, New York, NY, Chapter 18, pgs 355-379, 2001.
14. ***Clevenger CV** and Kline JB: Prolactin receptor signal transduction. *Lupus* 10:706-718, 2001.
15. **Clevenger CV:** An old epithelial cell never dies, it just agonesces away. (A research news update of *Nature* 409:633, 2001). *Trends Endocrinol Metabol,* 12:183-184, 2001.
16. ***Clevenger CV**, Furth PA, Hankinson SE, Schuler LA: The role of prolactin in mammary carcinoma. *Endocrine Reviews* (Issue's featured cover art), 24:1-27, 2003.
17. ***Clevenger CV**: Nuclear localization and function of polypeptide ligands and their receptors: A new paradigm for hormone specificity within the mammary gland? *Breast Cancer Research,* 5:181-187, 2003.

* = Peer reviewed.